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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,288	03/10/2004	Marlene M. Darfler	40970-0002	9373

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WASHINGTON, DC 20004

EXAMINER
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PETERSEN, CLARK D

ART UNIT	PAPER NUMBER
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1657

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

**Application No.**

10/796,288

**Applicant(s)**

DARFLER ET AL.

**Examiner**

Clark D. Petersen

**Art Unit**

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 18-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of Group I, claims 1-17, in the reply filed on 14 November 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' election of the species the detergent Triton X and the proteolytic enzyme trypsin is acknowledged.

Claims 18-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups, there being no allowable generic or linking claim. Election was made effectively **without** traverse in the reply filed on 14 November 2006.

The requirement is still deemed proper and is therefore made FINAL.

### *Specification*

The use of the trademark Liquid Tissue has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology (for example, in Figs. 1, 2, and 3).

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "heating a composition....at a temperature and time sufficient to *negatively affect protein cross-linking* in said biological sample". The italicized phrase does not make clear if Applicants intend the reversal of crosslinking induced by formaldehyde, for example, or breaking of specific crosslinked bonds in protein sample, or another intended purpose.

Claims 5 and 6 recite that the biological sample is heated to a specific temperature and time, however it is not specified at what point in the method this step occurs, i.e., it is unclear if claims 5 and 6 refer to step (a) of claim 1, or to any other time point in the method.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 7-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Banerjee et al (Biotechniques, 1995, from Applicants' IDS).

Banerjee et al teach a method of retrieving useful analytes from paraffin-embedded tissue samples. They teach that one can make a lysate from serial sections from archived paraffin embedded blocks. Sections were placed in microfuge tubes and microwaved to separate the paraffin from the tissue section (see "Microwave Treatment", p. 770). Paraffin melts at 56 degrees C, a temperature which can "negatively affect" formaldehyde crosslinking of proteins. The tissue samples came from pancreatic and Syrian hamster kidney tissue, reading on instant claim 2 (see p. 772, col. 2). Once free of paraffin, samples were digested by Proteinase K overnight at 42 degrees C, or 3 hr at 55 degrees C, reading on instant claims 7, 8, and 13. Before heating the sample and removing paraffin, the authors crushed the tissue in a buffer comprising Tris pH 8.5, reading on instant claims 4 and 14. All steps, i.e. heating and protease digestion, are carried out in the presence of 0.5% Tween-20, reading on instant claims 9, 10 and 12 (see p. 770 col. 1; see "Microwave Treatment" and Proteinase Digestion and Analysis of DNA Samples"). They teach that the samples can be extracted with phenol/chloroform/isoamyl alcohol, which can separates cell lysates into various fractions that a skilled artisan knows can be used for various biochemical assays, for example a DNA pellet and protein fraction (see p. 772, col. 2).

Therefore the teachings of Banerjee are deemed to anticipate the instant claims 1-4 and 7-17.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banerjee et al in view of Ikeda et al (J Histochem Cytochem, 1998).

The teachings of Banerjee et al are discussed above and applied as before.

Banerjee et al do not expressly teach deparaffinizing samples with an organic solvent.

Banerjee et al do not expressly teach heating a sample in incubation buffer comprising Triton X-100.

Banerjee et al do not expressly teach heating a sample to 80-100 degrees C for 10 min to 4 hr.

Ikeda et al teach that one can extract proteins from formalin-fixed, paraffin-embedded tumor samples. In particular Ikeda et al teach that one can pretreat samples with xylene to remove paraffin. Subsequently they add RIPA buffer to samples, which comprises 1% Triton X-100, and incubate the samples for various times ranging between 20 min and 2 hr at temperatures between 60 and 100 degrees C (see "Protein Extraction, p. 398 col. 2 to p. 399 col. 1). For example, they specifically set conditions for one trial at 100 degrees C for 20 min (see p. 399, col. 1, top paragraph). They teach

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that these methods allow for detection of various proteins associated with cancerous phenotype by Western blot (see Discussion, p. 401, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to extract various biomolecules from paraffin embedded tissue using xylene deparaffinization followed by heat treatment in a buffer comprising Triton X-100, because Banerjee et al teach that one can make a multi-molecule lysate from formalin-fixed, paraffin-embedded tissue, and Ikeda et al teach that proteins can be efficiently extracted from such tissue by deparaffinizing in xylene, followed by heat treatment in a buffer comprising Triton X-100.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to prepare a biomolecule lysate from paraffin embedded tissues by removing paraffin with xylene and heat-treating the samples in a buffer comprising Triton X-100.

Claims 1-4 and 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banerjee et al in view of Kanai et al (Res Vet Sci, 1998).

The teachings of Banerjee et al are discussed above and applied as before.

Banerjee et al do not expressly teach that one can use trypsin to effectively treat formalin fixed tissue for detection of analytes.

Kanai et al teach that trypsin is a useful enzyme for treatment of formalin fixed tissue samples. They teach that one can incubate deparaffinized tissue sections with 0.25% trypsin at 37 degrees Celsius for 30 to 120 min, and perform

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immunohistochemistry on those sections, demonstrating an improvement of immunoreactivity of trypsin-treated tissue (see Materials and Methods, p. 58, col. 2 – “Enzymatic pretreatment”; see Fig. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to include trypsin in the digestion of formalin-fixed tissue because Ikeda et al demonstrate that treatment with trypsin improves antigen exposure, and therefore increased sensitivity in detection of analytes of interest.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include trypsin in a digest of de-paraffinized, formalin fixed tissue to obtain a lysate for analyte detection.

Claims 1-4 and 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banerjee et al in view of Francis et al (Biochem J, 1980).

The teachings of Banerjee et al are discussed above and applied as before.

Banerjee et al do not expressly teach the use of Triton X-100 in the step of proteinase digestion of a de-paraffinized sample.

Francis et al teach that tissue samples can be treated with trypsin and Triton X-100. Francis et al teach that it is more effective to liberate membrane protein fragments from microsomes when both trypsin and Triton X-100 are included to solubilize and fractionate proteins (see “Extraction by tryptic digestion in the presence of Triton X-100”, p. 572, col. 1 bottom, for example). They report that a particular protein activity could not be liberated from microsomes by either trypsin or Triton X-100 alone, but when the

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two reagents are combined with microsomes, the protein could be separated (see p. 575, col. 2 last paragraph to p. 576, col. 2, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to include Triton X in a method of solubilizing tissue, because Banerjee et al teach that biomolecule lysate can be obtained from formalin-fixed tissue by treatment with proteinase and detergent, and Francis et al teach that some proteins, in particular membrane proteins, can be more effectively purified from lipid fractions by including both trypsin and Triton X-100 in the solubilization reagent.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to prepare a biomolecule lysate from paraffin-embedded, formalin fixed tissue by treating the tissue with trypsin and Triton X-100.

### ***Conclusion***

No claims are allowed.

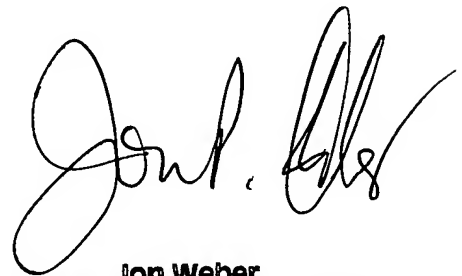
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP  
2/1/2007

A handwritten signature in black ink, appearing to read "Jon Weber", with a stylized flourish at the end.

**Jon Weber**  
**Supervisory Patent Examiner**